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SOME REMARKS

ON THE

NATURE AND TREATMENT

OF

PULSATING THYROID GLAND,

WITH EXOPHTHALMOS

("GRAVES' DISEASE").

BY

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SOME REMARKS
ON THE
NATURE AND TREATMENT OF PULSATING THYROID GLAND,
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(“GRAVES’ DISEASE.”)

THE deep interest which attaches to this distressing affection, the fact of its comparatively unfrequent occurrence, and of the subject not being hackneyed, induces me to contribute the following brief observations to the pages of this valuable Journal. The affection now generally termed “Graves’ Disease,” viz., palpitation with visible pulsation in the carotids and thyroid body, with exophthalmos, has been treated of more or less, by writers at home and abroad. At home mainly by Graves,^a Stokes,^b Marsh,^c Banks,^d Begbie,^e Mackenzie,^f and Laycock;^g whilst the foreign contributors are Withusen,^h Græfe,ⁱ Desmarres,^j Arlt,^k Helft,^l Bruck,^m Basedow,ⁿ Trousseau, and others. Among the most remarkable phenomena of this affection are the cardiac pulsations, which exceed in frequency and violence those commonly met with in organic disease of the heart. They are so rapid and tempestuous in some cases it is difficult to define their frequency. The carotids and arteries of the upper extremities partake of this excessive vascular excitement, whilst the circulation in the lower extremities is below par.

^a Clinical Medicine.

^b Diseases of the Heart and Aorta.

^c Dub. Journal.

^d Dub. Hosp. Gazette, 1855.

^e Edinburgh Med. Journal, 1863.

^f Diseases of the Eye.

^g Edinburgh Med. Journal.

^h Bibliothek für Læger.

ⁱ Archiv. iii.

^j Gazette des Hôpitaux.

^k Krankheiten des Auges.

^l Casper’s Wochenschrift, 1849.

^m Heidelberger Medicinische Annalen.

ⁿ Med. Times and Gazette, 1862.

Occasionally the external jugular veins become prominent, and borrow pulsation from the adjacent vessels, whilst the thyroid gland becomes enlarged, pulsates, and conveys *fremissement* to the hand, a musical murmur being occasionally audible. Next comes the exophthalmia, the eyes (or eye, as has been once or twice observed) becoming prominent, in some cases painful on being handled, and accompanied with imperfect vision. Superadded to these objective symptoms we meet with mental depression in various aspects, globus, vertigo, tinnitus, and other such distressing signs.

Bruek and Basedow found in some of their patients a hysterical condition, with morbid craving for amusement and dissipation, but such has not been my experience.

With respect to the exciting cause of this malady, among the six cases which form the subject of this paper, of which five were females and one male—in three of the female cases the occasion of the disease was attributed to shocks from sudden deaths or mental emotion with subsequent depression; in another female case profuse menorrhagia; and in the fifth, loss of independence and social position seemed the origin of the affection; whilst in the instance of the male, the most rational explanation of the occurrence of the disease was excessive sexual indulgence.

Withusen (whose valuable paper on this subject has been translated by Dr. W. D. Moore, of this city, in the *Dublin Medical Press*, Vol. XLII.) tells us that the disease has been referred to causes which have had a depressing influence on mind or body, such as long-continued or very violent mental affections, from over application to study, still more frequently to weakening discharges—as hemorrhage, diarrhea, excessive lactation or leucorrhea.

The following details of a case under my observation will exemplify the symptoms and physical signs of this distressing malady:—Mrs. C—, aged thirty-four, a slight spare woman, consulted me about three years ago for general nervous and hysterical affections, palpitation and globus being chiefly complained of. On further inquiry I found she had been suffering from profuse menorrhagia for the previous eighteen months, that for the six months before my seeing her she remarked her neck becoming thick and swollen, and that at times she was afflicted with violent throbbing in her head. These symptoms abated from time to time, but on their recurrence they always seemed aggravated, till the eyes became staring and restless, and the catamenia, instead of

being excessive, became deficient in quantity and colourless, the subjective symptoms keeping pace, more especially the complaint of suffocation, and painful throbbing along the neck and each side of the head. The heart's action at this stage of the disease was over 140 in the minute, and this excessive cardiac pulsation was visible, and could be heard along the great vessels, accompanied with a loud souffle. The thyroid gland was enlarged, the right lobe may be said to have increased a little, it was certainly larger than the left, and distinct pulsation, with *fremissement*, could be felt all over it; the patient was also suffering from partial aphonia. The exophthalmia was most remarkable, the pupils were dilated, and the eye generally restless and fidgetty. The sclerotic coat of a muddy yellow hue, whilst the patient complained of dimness and partial loss of vision, with pain on the eye being touched or handled.

This case gives a general view of the symptoms and physical signs which this affection presents. In the other cases which I carefully observed there were some variations. For instance, in the case of a tall handsome woman, about thirty years of age, the pulsations became so frequent, irregular, and tempestuous, that it was impossible to determine their frequency with accuracy, whilst the pulsating carotids stood out as thick as ordinary sized middle fingers. The thyroid body was enlarged and pulsated, but it did not attain a great size; the right lobe, however, was larger than the left. There was no evidence of spanemia about this patient; but as the disease progressed there was manifest diminution in the circulation inferiorly, and the menstrual function, which had been irregular from the commencement, eventually became suppressed.

This case proved fatal, with all the symptoms of valvular patency, occasional delusions having occurred before death.

The *third* case was a young woman about twenty-seven years of age, florid and muscular. In this case, the exophthalmos was very remarkable, and the eyeballs painful on being touched; the right half of the thyroid gland was larger than the left, and the cardiac pulsations exceeded 150 in the minute; the catamenia were deficient, but the improvement in the patient took place, *pari passu*, with the menstrual restoration.

In the *fourth* case that of a young married woman, staring disfiguring exophthalmia, imperfect vision, and general spanemia, with thyroid enlargement and palpitation, were the prominent symptoms, all of which seemed to abate after the occurrence of pregnancy.

The *fifth* case occurred in a married woman, 30 years of age, who had never borne children, and who suffered from total suppression of the menses, the exophthalmia in this case was revolting; the right half of the thyroid gland was larger than the left, and there was well nigh complete aphonia. In this case also the general improvement in the other symptoms was coeval with the restoration of the catamenia.

The last case I shall here adduce was that of a deaf mute, aged thirty-one, who presented this affection in an aggravated form, but which yielded readily to free doses of digitalis. Of these six cases only one has proved fatal, with œdema, ascites, and all the other symptoms and signs of valvular insufficiency and general cardiac dilatation. Such a condition corresponds with the pathology of this disease as described by Sir H. Marsh and others. In Sir Henry's case both auricles, particularly the left, were dilated and hypertrophied, and the auriculo-ventricular valves of both sides exhibited thickened margins. In Professor Smith's case there was hypertrophy and dilatation of the left ventricle.^a Dr. Banks^b found the thyroid gland enlarged to four or five times its natural size, the right lobe larger than the left, and the body solid and lobulated, a section disclosing numerous cysts. The heart was as large as that of an ordinary sized man (the patient being a woman under the middle size); its valves were free from disease, with the exception of slight thickening of the anterior edge of the mitral valve. The lungs were congested, the liver appeared in an early stage of cirrhosis, the spleen was large and congested, the brain softer than natural, the kidneys had undergone the changes usually observed in the early stage of Bright's disease, albumen having been present in the urine during life, whilst hypertrophy of the left ventricle, without dilatation, existed; in addition a thickened, rigid, uneven condition of the semilunar valves. The right side of the heart was dilated without hypertrophy; much fat was found in the heart, and atheromatous deposit in the aorta and its branches—even in the arteries of the brain, the ophthalmic, and ciliary.

^a Hensinger found hypertrophy and dilatation of the left ventricle with great flaccidity of the muscular substance, whilst Prael met with the same condition of the left side of the heart, with atheromatous degeneration engaging the endocardium and aortic arch, with extensive softening of the brain. Casper *Wochenschrift*, 1851. Newman reports a case in which vision was lost several months before death. *Deutsche Klinik*, 1853.

^b *Dublin Hospital Gazette*, 1855.

The thyroid body was enlarged and hypertrophied, its vessels dilated and tortuous, and in some cases aneurismatically.

Cushions of fat have been found, in some cases, behind the eyes, which generally present the appearance of deep-seated inflammation.

In the case of a woman who died of apoplexy in the Hotel Dieu,^a Professor Trousseau found the superior part of the sympathetic system in a state of marked congestion; the texture of the ganglia had undergone alteration, a portion of their substance being replaced by cellular tissue; and in Dr. Cruise's case, the *post mortem* examination of which he made most carefully, with the assistance of Dr. Robert M'Donnell, the inferior cervical sympathetic ganglia were almost obliterated, being supplanted by cellular and adipose tissue.

These latter observations on the nervous pathology of this affection are most important; and I have no doubt when further extended to the nerves of the cord in general, and those of the cilio-spinal region in particular, increased light will be thrown on the nature of this interesting disease.

With respect to the enlargement of the thyroid body, which occurred in these cases I have detailed, it did not attain the size of ordinary goître. Some have asserted that there is no observable difference between this thyroid enlargement and that of ordinary bronchocele; but such is not my belief; in none of the above cases did the tumour attain a very great size, and after a time it became stationary, the right lobe being larger than the left, and in most instances the thyroid enlargement sensibly decreasing, *pari passu*, with the decrease in the palpitation; of course where the disease is of long standing, and the gland has become thickened and hypertrophied from a varicose state of its vessels, such a favourable condition of things is not to be expected. Still the fact of the decrease of the thyroid body keeping pace with the diminution in the cardiac pulsations goes far, in my mind, to refute M. Piorry's theory, viz., that the thyroid enlargement is the starting point from which the other symptoms result—the pressure from the increased gland causing dyspnea, cardiac embarrassment, and exophthalmia.

But the question naturally suggests itself, to what are all these formidable symptoms due and owing? and on this point there is a great diversity of opinion.

Dr. W. Begbie holds that the true pathology of the exophthalmos

^a Journal of Practical Medicine and Surgery, 1864.

and enlarged thyroid body, found associated with cardiac palpitation and vascular pulsations, is due both to the blood and nervous system, but that the condition of the circulating fluid is the main agent, viz.: that an altered state of the blood, stopping short of what is generally termed anemia (but in many cases amounting to this condition) acts directly on the nerves of the blood-vessels and on the cardiac nerves; that as a sequence their movements are seriously affected, the results being—dilatation of blood-vessels, arteries, and veins, and of the chambers of the heart itself. He believes that for a long period the bronchocele is, or may be, vascular enlargement and dilatation, but in course of time hypertrophy and structural degeneration of the gland ensues. The exophthalmos depending upon vascular congestion and dilatation of the ophthalmic vessels with effusion of serum into the post orbital cellular tissue. Lastly, he concludes that a plan of treatment, with a view to an improvement in the condition of the blood, and simultaneously in the state of the nervous system, is successful in effecting a cure, provided radical structural changes have not taken place.

Trousseau, on the contrary, does not consider "Graves' disease" a cachexia, as chlorosis, or albuminuria, and he considers the co-existence of anemia as only consecutive to the disturbance of nutrition, albuminuria being a very rare symptom of exophthalmic bronchocele. He believes the disease to be a neurosis, somewhat analogous to hysteria, characterized by local determinations, having its origin in some modification of the vaso-motor (sympathetic) system. The palpitation, enlargement, and pulsation of the thyroid body, and the exophthalmos are direct consequences of this; and the diarrhea, the diuresis, and diaphoresis are due to congestion of the glandular apparatus—the irregularity of the menstrual function being caused by the deficiency of blood in the utero-ovarian system; and if this is restored, either by pregnancy or other causes, many of the symptoms of the disease disappear, as if the return of the uterine hyperemia caused the morbid congestions of the other organs to cease. Dr. Laycock attributes this affection to nervous agency, whilst Dr. Stokes has not found this disease associated with any form of carditis, and concludes that it is a special form of cardiac neurosis which may eventuate in organic disease. Whether the nervous excitement is propagated to the arteries in the neck is a question he has often proposed to himself, for there is something in their action which he considers cannot be altogether explained by

the force of the heart. The double pulsation of the arteries of the neck, and those alone, he considers another evidence of local vascular excitement. Both Henoch and Stokes agree that this condition is not attended with fever, nor with physical signs or general symptoms of cardiac inflammation.

Now, although many of the most prominent symptoms of this affection, as palpitation, menstrual suppression, and mental anxiety are compatible with anemia, still I am not prepared to admit such to be the exciting cause of this disease. In four of the cases I have adduced the appearance of the patients was not spanemic; on the contrary, three of them might be called florid and well developed, and when ferrugineous preparations were exhibited they proved ineffectual.

In this view of the question I am not singular; for whilst Withusen admits that in a great proportion of cases there was well marked anemia, with suppression of the menses, and cardiac symptoms such as would suggest the inference that this morbid condition stands in direct relation to the phenomena of Graves' disease; still, he goes on to say—if this blood disease had always evinced itself in a greater or less degree we should have progressed in our knowledge of this affection; but such is by no means the case, as numerous instances could be shown where not a trace of anemia was present; on the contrary, the patients were blooming, active, and plethoric, and where the remedies usually employed in anemia were found absolutely useless. Nor does Henoch regard anemia as an indispensable element in the development of the disease.

For my own part I consider the origin of this affection to be essentially nervous, in which the vaso-motor system plays the most conspicuous part. When we consider that the motor fibrils of the heart are derived from the sympathetic as well as from the spinal nerves; and as Professor Moleschott has shown that the heart is animated by four very excitable nerves—two vagi and two sympathetic, having a peculiar consensus, so that the state of irritation or over-excitement which is produced in one of the nerves is transmitted to the other three; again, branches from the inferior cervical sympathetic supply the thyroid body and larynx; such being the nervous distribution we may easily reconcile palpitation, pulsation of the carotids and thyroid body, with any vaso-motor irritation along this important region. Then comes the question of exophthalmia, dilated and restless pupils, &c. It is now an admitted fact that there are two antagonistic set of fibres in the

iris—the circular or contracting fibres surrounding the pupil being influenced by the third cranial nerve, whilst the dilating fibres of the pupil are influenced by the sympathetic.^a Drs. Budge and Waller, however, have shown that the fibres going to dilate the pupil originate from the spinal cord, from the region termed the “cilio-spinal,” which extends from the sixth cervical to the fourth dorsal; and Brown-Séquard gives even a more extensive origin to these; and with respect to the vaso-motor influence of these nerves, he has discovered that it is derived chiefly from the spinal cord, by the last cervical and two highest dorsal nerves. Schiff^b goes still further, maintaining that the dilating fibres of the iris originate from the highest cervical nerves, even from the medulla oblongata. Under any circumstances any excitation employed along this cervico-dorsal region will cause increased vaso-motor action—hence exophthalmos and dilatation of the pupil. But it may be urged might not this dilatation of the pupils be attributable to some deficiency in the nervous action of the third pair, which would lessen the normal counteracting contractile action of the iris, and hence dilatation. This, I think, can readily be met by the fact that there is no evidence of disease of the brain or symptoms of compression. In short the conclusion most satisfactorily arrived at in my mind is, that the cardiac pulsations, pulsating thyroid gland, and carotids, with exophthalmos, dilated and restless pupils, are due to the increased vaso-motor or sympathetic action. Further, the experiments of Schiff, Bernard, and others go to prove that the disease of the sympathetic system induces in the organs more immediately under its influence changes which eventuate in atrophy; the texture of the various organs, from impaired nutrition, being replaced by adipose and cellular tissue. Such being the condition these cases usually present. Again, when we turn to the condition of the lower extremities, we find this abnormal vascular excitement superiorly starving the lower extremities of their due supply of blood, and hence the menstrual irregularities which ensue; the restoration of this function to as nearly a healthy standard as possible being a sure indication of general amendment. Withusen, however, mentions one case in which menstruation was checked for two Summers; on the first occasion it was absent for five months without any apparent change in the patient's state,

^a Vierordt's Archiv. Fur Physiol. Heilkunde, 1852.

^b Untersuchung z Physiologie des Nervensystems.

while on the last occasion the visible improvement in the case coincided with the arrest of the function. Such an instance has not come under my observation, but in one of my cases pregnancy seemed to exert a favourable influence. With respect to the prognosis of this disease, the more I see of it the more hopefully I am inclined to regard it. That the affection has proved fatal more rapidly in men than in woman is generally admitted; but this I cannot endorse from my own experience, as all the cases I have seen occurred in females, with one exception, and as yet, as far as I can learn, only one of these cases has proved fatal. In some of the others perfect recovery seems to have taken place, whilst in one case, which I have frequent opportunities of observing, the cardiac distress, carotid and thyroid pulsations have ceased, but the gland still remains enlarged, with partial exophthalmos.

The character of the affection, without doubt, is very prone to relapses, which sooner or later must entail organic changes incompatible with length of life; still with common care, and due prophylactic means being adopted, these relapses may, to a great extent, be anticipated. Among the most important of these means I should consider the distraction of the patient's attention as far as possible from what may have proved, in his or her case, the special exciting cause, for which change of scene and society will be found indispensable. As regards the special treatment of the disease, bleeding is inadmissible; but Withusen has found the application of a leech or leeches to the external cavities of the eye useful where there was much pain and tension associated with the exophthalmos. Of the therapeutical remedies I have found the tincture of digitalis, in doses of from fifteen to twenty-five drops—three or four times a-day, most efficacious—combining it with iron where I had reason to believe *spanemia* existed. The extract of digitalis may also be applied locally over the precordial region. Bromide of potassium I look upon as a valuable agent in these cases, but I should give it in much larger doses than those usually directed in books—say from fifteen grains to half a drachm, three or four times daily; its special therapeutical properties I am not prepared to define, but it seems to me to exert a sedative and equalizing effect on the vaso-motor system generally, more especially in restoring the uterine functions to their normal condition. The use of iodides, both internally and externally, have proved equally inefficacious in my hands. Yet Professor Trousseau inclines to the belief that iodine, internally and externally, combined with hydropathy, will, perhaps, be found the most useful

resource of the therapist in this singular disease. Iron, *per se*, has also disappointed me. I think in these cases it would be well to keep up counter-irritation along the cilio-spinal region either by means of small blisters or liniments, such as the compound camphor or soap liniments, with belladonna or chloroform.

